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09/785,559	02/16/2001	Karl-Heinz Boven	WITTE-011XX	3534

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EXAMINER

BEISNER, WILLIAM H

ART UNIT PAPER NUMBER

1744

DATE MAILED: 12/19/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Applicati n No.

09/785,559

Applicant(s)

BOVEN ET AL.

Examiner

William H. Beisner

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 15 August 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-53 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-53 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 February 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112*

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, "said electrodes" is indefinite and lacks antecedent basis because the claim previously recites "at least one electrode" while the latter language implies plural electrodes. It is not clear if the claim language encompasses a device with a single electrode or plural electrodes.

In claims 2-9, "said electrodes" lacks antecedent basis for the same reasons as set forth above with respect to claim 1.

In claims 10, 11 and 14, it is not clear if the claim is referring to the same "at least one electrode" of claim 1. It is suggested that the claim language be amended to recite --said at least one electrode--.

In claim 12, "said carrier" lacks antecedent basis. Claim 1 does not employ this claim language.

In claim 19, "said at least one measuring electrode" lacks antecedent basis. Note claim 19 depends from claim 1 not claim 16.

In claim 24, "said at least two measuring electrodes" lacks antecedent basis. Note claim 24 depends from claim 16 not claim 23.

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Should claim 25 depend from claim 23 or 24 rather than claim 21? It is not clear because the claim does not recite “said at least one electrode” or “said at least two electrodes”.

In claim 26, “said second plane” lacks antecedent basis. Claim 26 depends from claim 24 not claim 25. Also if changed to depend from claim 25, “said first plane” would lack antecedent basis. Clarification and/or correction is requested.

In claim 27, “said carrier” lacks antecedent basis.

In claim 29, “said perfusion inlet” lacks antecedent basis. Claim 29 depends from claim 16 not claim 27 or 28. Furthermore, claims 27 and 28 do not recite “a perfusion inlet”.

In claim 30, “said perfusion inlet” and “said measuring electrodes” lack antecedent basis. Note claim 30 depends from claim 14. Note, claim 29 recites a perfusion inlet and claims 27 and 28 recite a perfusion conduit.

In claims 31, 33 and 34, “said perfusion inlet” lacks antecedent basis. Note claim 27 recites a perfusion conduit.

In claims 35 and 36, “said at least one storage container” lacks antecedent basis. Note claim 33 recites “a plurality of storage containers”.

How does claim 37 differ from claim 28, if at all?

In claim 38, “said perfusion outlet” lacks antecedent basis. Note claim 29 recites a perfusion inlet. It is not clear what is intended by the last line since the claim already recites a perfusion outlet. Also “said perfusion conduit” lacks antecedent basis.

In claim 42, “said perfusion inlet”, “said perfusion outlet”, “said at least one measuring electrode” and “said perfusion conduit” lack antecedent basis.

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In claim 43, "said at least one measuring head" lacks antecedent basis. Note claim 1 merely recites "a measuring head".

In claim 48, "said actuator" lacks antecedent basis. Note claim 48 depends from claim 47 and claim 1 not claim 43.

In claims 49-51, it is not clear if the well plate is being claimed as part of the device. Currently the language appears to imply that the device is capable of being used with a well plate and that the actuator includes a bar code reader.

### ***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
  2. Ascertaining the differences between the prior art and the claims at issue.
  3. Resolving the level of ordinary skill in the pertinent art.
  4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

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evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-28, 31-37, 40, 41, 43, 46, 49, 52 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takeshita et al.(US 6,277,559) in view of Olesen et al.(WO 98/50791).

The reference of Takeshita et al. discloses an electrophysiological measurement device which includes a chamber for holding a cell which is impaled by electrodes (3 and 4) and perfusion system (9, 14, 15, 20) (See Figures 1 and 6). The reference discloses the use of glass electrodes which include silver coated with silver chloride wires (See column 6, lines 1-8).

While the reference discloses the use of electrodes for impaling the cell, the reference is silent as to a carrier or support for the electrodes.

The reference of Olesen et al. discloses that it is known in the art to mount the electrodes of an electrophysiological measuring device on a micromanipulator device (see page 20). The reference discloses that the micromanipulator can support a plurality of electrodes. The reference also discloses patch clamp electrodes with a resistance of 2-5Mohms (See page 30).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to mount the electrodes of the primary reference of a micromanipulator as suggested by the reference of Olesen et al. for the known and expected result of providing a means recognized in the art for automating the positioning of the electrodes relative to the cells to be impaled for detection.

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result of providing a means recognized in the art for automating the positioning of the electrodes relative to the cells to be impaled for detection.

With respect to the manner in which the electrode is attached to the micromanipulator would have been merely an obvious matter in design choice based on considerations. It would have been obvious to allow the electrodes to be replaceable while reusing the manipulator carrier or it would have been obvious to provide an integrated unit if the system is to be reused by cleaning rather than by replacement of electrodes.

While the reference discloses the electrodes mounted at an angle relative to vertical, the reference is silent as to the angle. However, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to determine the optimum angle of the electrodes while providing a reliable means for impaling the cells to be measured.

With respect to the distance between the tips of the electrodes, it would have been obvious to one of ordinary skill in the art to maintain the tips of the two electrodes at a distance which allows both electrodes to impale a single cell while preventing the electrodes from interfering with one another.

With respect to the claimed current and measuring amplifier, see Figure 1 of Takeshita et al. and page 23 of Olesen et al.

With respect to the number of reference and measuring electrodes, as discussed by both Takeshita et al. and Olesen et al., it would have been obvious to one of ordinary skill in the art to determine the optimum electrode configuration based merely on the specifics of the measurements to be performed.

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With respect to the use of pumps and solution reservoirs, the reference of Olesen et al. discloses (See Figure 1) a perfusion system which is known and would have been obvious for the known and expected result of testing the cells to different types of chemical stimulations.

7. Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over Takeshita et al.(US 6,277,559) in view of Olesen et al.(WO 98/50791) and Byrne et al.(WO 00/34776).

The combination of the references of Takeshita et al. and Olesen et al. has been discussed above.

While the references disclose mounting the electrodes on a micromanipulator, the references do not disclose the use of a plurality of measuring heads on a single manipulator.

The reference of Byrne et al. discloses that it is known in the art to provide a plurality of measuring electrodes on a single carrier while measuring a plurality of cells in a plurality of difference measuring chambers (See Figure 24).

In view of this teaching, which using a plurality of cell chambers or wells, it would have been obvious to one of ordinary skill in the art to provide a single micromanipulator which carries a plurality of detection electrode sets for the known and expected result of allowing a plurality of cells to be measured simultaneously and be simultaneously impaled using a single manipulator.

8. Claim 47 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takeshita et al.(US 6,277,559) in view of Olesen et al.(WO 98/50791) and Farb et al.(US 6,048,722).



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The combination of the references of Takeshita et al. and Olesen et al. has been discussed above.

The claims further require that the carrier includes a cell injection device.

The reference of Farb et al. disclose that it is known in the art to provide electrophysiological measurement device with cell injection devices (See column 3, lines 15-24).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to include a microinjection needle in the manipulator device for the known and expected result of providing a means recognized in the art for injecting nucleic acids into the cells as is suggested by the reference of Farb et al.

9. Claims 50 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takeshita et al.(US 6,277,559) in view of Olesen et al.(WO 98/50791) and Carr et al.(US 5,888,825).

The combination of the references of Takeshita et al. and Olesen et al. has been discussed above.

The claims differ by reciting that individual cell receptacles within the device are identified by bar codes and the manipulator includes a bar code reader.

The reference of Carr et al. discloses that it is well known in the art when monitoring a plurality of reaction vessels to identify each receptacle using bar codes and to use a bar code reader on the device monitoring the reaction in reach vessel (See column 4, line 65 to column 5, line 5).

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In view of this teaching, it would have been obvious to one of ordinary skill in the art to provide the micromanipulator with a bar code reader for identifying a selected reaction chamber when performing a plurality of tests as is disclosed in the reference of Olesen et al. (See Figures 13 and 16).

### ***Allowable Subject Matter***

10. Claims 29, 30, 38, 39, 42 and 45 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

11. The following is a statement of reasons for the indication of allowable subject matter:

The above claims would be allowable because the prior art of record fails to teach or fairly suggest the combination of the electrodes for performing an electrophysiological measurement and perfusion inlets and outlet on a single measuring head which is moved relative to the receptacle which contains the cell to be measured.

### ***Conclusion***

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

The following references are cited as being of interest: Furusawa et al.(US 4,270,838) which is drawn to a micromanipulator for cell measurements; Mathes et al.(US 6,461,860) which is drawn to holders for cell measuring electrodes; Kudryavtse (DE 3134964) which is drawn to a

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cell penetration micromanipulator; and Hitachi (JP 11-299496) which is drawn to a cell penetration device.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 703-308-4006. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:40am to 4:10pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Warden can be reached on 703-308-2920. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9310 for regular communications and 703-872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0661.



William H. Beisner  
Primary Examiner  
Art Unit 1744

WHB  
December 16, 2002